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PTO/SB/08A/B 08-03)  
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| Substitute for form 1449PTO   |   | <b>Complete if Known</b> |                        |                        |              |
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>(use as many sheets as necessary) |   | Application Number       | 10/661,097             |                        |              |
|   |   | Filing Date              | September 12, 2003     |                        |              |
|   |   | First Named Inventor     | Andrew Vaillant et al. |                        |              |
|   |   | Art Unit                 | 1635                   |                        |              |
|   |   | Examiner Name            | Jane J. ZARA           |                        |              |
| Sheet   | 1 | of                       | 13                     | Attorney Docket Number | 16051-6US CC |

| U.S. PATENT DOCUMENTS |                       |  |                                |  |  |
|-----------------------|-----------------------|--|--------------------------------|--|--|
| Examiner Initials*    | Cite No. <sup>1</sup> | Document Number                            | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines Where<br>Relevant Passages or Relevant<br>Figures Appear |
|                       |                       | Number - Kind Code <sup>2</sup> (if known) |                                |  |  |
| J3                    |                       | US-5,563,050                               |                                |  |  |
|                       |                       | US-6,506,559                               |                                |  |  |
|                       |                       | US-5,023,252                               |                                |  |  |
|                       |                       | US-5,580,859                               |                                |  |  |
|                       |                       | US-4,806,463                               |                                |  |  |
|                       |                       | US-5,248,670                               |                                |  |  |
|                       |                       | US-5,591,720                               |                                |  |  |
|                       |                       | US-5,952,490                               |                                |  |  |
|                       |                       | US-5,998,602                               |                                |  |  |
|                       |                       | US-6,184,369                               |                                |  |  |
|                       |                       | US-5,264,423                               |                                |  |  |
|                       |                       | US-5,276,019                               |                                |  |  |
|                       |                       | US-6,316,190                               |                                |  |  |
|                       |                       | US-5,218,103                               |                                |  |  |
|                       |                       | US-5,684,148                               |                                |  |  |
|                       |                       | US-5,452,496                               |                                |  |  |
|                       | US-5,278,302          |  |                                |  |  |
|                       | US-5,750,666          |  |                                |  |  |
|                       | US-5,602,244          |  |                                |  |  |
|                       | US-5,508,270          |  |                                |  |  |

| FOREIGN PATENT DOCUMENTS |                       |  |                                |  |  |
|--------------------------|-----------------------|--|--------------------------------|--|--|
| Examiner Initials*       | Cite No. <sup>1</sup> | Foreign Patent Document<br>Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known) | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines<br>Where Relevant Passages<br>or Relevant Figures Appear |
| J3                       |                       | WO 03/02903  |                                |  |  |
|                          |                       | WO 99/32619  |                                |  |  |
|                          |                       | WO 01/75164  |                                |  |  |
|                          |                       | WO 92/03051  |                                |  |  |
|                          |                       | WO 94/17093  |                                |  |  |
|                          |                       | WO 94/02499  |                                |  |  |
|                          |                       | WO 94/26764  |                                |  |  |
|                          | WO 97/13499           |  |                                |  |  |

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| Examiner Signature |  | Date Considered | 12-12-06 |
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| J3                    |                          | US-4,469,863                               |                                |  |  |
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|                       |                          | US-5,256,775                               |                                |  |  |
|                       |                          | US-5,366,878                               |                                |  |  |
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|                       |                          | US-5,023,243                               |                                |  |  |
|                       |                          | US-5,130,302                               |                                |  |  |
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|                       |                          | US-5,378,825                               |                                |  |  |
|                       |                          | US-5,386,023                               |                                |  |  |
|                       |                          | US-5,489,677                               |                                |  |  |
|                       |                          | US-5,264,562                               |                                |  |  |
|                       |                          | US-5,264,564                               |                                |  |  |
|                       |                          | US-5,223,618                               |                                |  |  |
|                       |                          | US-5,770,713                               |                                |  |  |
|                       |                          | US-5,543,152                               |                                |  |  |
|                       |                          | US-4,426,330                               |                                |  |  |
|                       | US-4,534,899             |  |                                |  |  |
|                       | US-5,705,188             |  |                                |  |  |
|                       | US-5,013,556             |  |                                |  |  |

| FOREIGN PATENT DOCUMENTS |                          |  |                                |  |  |   |
|--------------------------|--------------------------|--|--------------------------------|--|--|---|
| Examiner<br>Initials*    | Cite<br>No. <sup>1</sup> | Foreign Patent Document                            | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines<br>Where Relevant Passages<br>or Relevant Figures Appear | † |
|                          |                          | Country Code 3 - Number 4 - Kind Code 5 (if known) |                                |  |  |   |
| J3                       |                          | WO 90/04384  |                                |  |  |   |
|                          |                          | WO 97/30731  |                                |  |  |   |
|                          |                          | EP 0 496 813 B1                                    |                                |  |  |   |
|                          |                          | EP 0 445 131 B1                                    |                                |  |  |   |
|                          |                          | WO 91/05545  |                                |  |  |   |
|                          |                          | WO 94/20073  |                                |  |  |   |
|                          |                          | WO 96/10391  |                                |  |  |   |
|                          | WO 98/39352              |  |                                |  |  |   |

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|                       |                          | Number - Kind Code <sup>2</sup> (if known) |                                |  |  |
| JP                    |                          | US-5,356,633                               |                                |  |  |
|                       |                          | US-5,213,804                               |                                |  |  |
|                       |                          | US-5,225,212                               |                                |  |  |
|                       |                          | US-5,540,935                               |                                |  |  |
|                       |                          | US-5,556,948                               |                                |  |  |
|                       |                          | US-6,316,190                               |                                |  |  |
|                       |                          | US-5,264,221                               |                                |  |  |
|                       |                          | US-5,665,710                               |                                |  |  |
|                       |                          | US-4,806,463                               |                                |  |  |
|                       |                          | US-5,248,670                               |                                |  |  |
|                       |                          | US-5,695,979                               |                                |  |  |
|                       |                          | US-5,591,623                               |                                |  |  |
|                       |                          | US-5,514,788                               |                                |  |  |
|                       |                          | US-5,652,355                               |                                |  |  |
|                       |                          | US-6,143,881                               |                                |  |  |
|                       |                          | US-6,346,614                               |                                |  |  |
|                       |                          | US-5,591,721                               |                                |  |  |
|                       |                          | US-6,608,035                               |                                |  |  |
|                       | US-3,687,808             |  |                                |  |  |
|                       | US-5,625,050             |  |                                |  |  |

| FOREIGN PATENT DOCUMENTS |                          |   |                                |  |  |                |
|--------------------------|--------------------------|---|--------------------------------|--|--|----------------|
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|                          |                          | Country Code3 - Number4 - Kind Code5 (if known) |                                |  |  |                |
| JP                       |                          | WO 99/14226                                     |                                |  |  |                |
|                          |                          | WO 96/40062                                     |                                |  |  |                |
|                          |                          | WO 97/04787                                     |                                |  |  |                |
|                          |                          | WO 04/02419                                     |                                |  |  |                |
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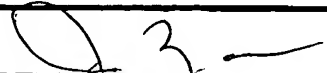
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|                       |                          | US-6,013,240                               |                                |  |  |
|                       |                          | US-5,837,449                               |                                |  |  |
|                       |                          | US-6,177,246                               |                                |  |  |
|                       |                          | US-5,670,634                               |                                |  |  |
|                       |                          | US-2003/232435                             |                                |  |  |
|                       | US-2003/0119019 A1       |  |                                |  |  |
| ✓                     |                          | US-2003/0162225 A1                         |                                |  |  |
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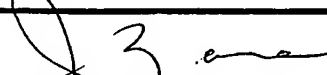
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| NON PATENT LITERATURE DOCUMENTS |                       |   |                |
|---------------------------------|-----------------------|---|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published  | T <sup>2</sup> |
| 83                              |                       | ADJOU <i>et al.</i> , "A novel generation of heparan sulfate mimetics for the treatment of prion diseases", 2003, <i>J. Gen. Virol.</i> 84:2595-2603.   |                |
|                                 |                       | AGRAWAL, "Importance of nucleotide sequence and chemical modifications of antisense oligonucleotides", 1999, <i>Biochim. Biophys. Acta</i> 1489:53-68.  |                |
|                                 |                       | AGRAWAL and KANDIMALLA, "Antisense therapeutics: Is it as simple as complementary base recognition?", 2000, <i>Mol. Med. Today</i> 6:72-81.   |                |
|                                 |                       | AKHTAR <i>et al.</i> , "The delivery of antisense therapeutics", 2000, <i>Advanced Drug Delivery Reviews</i> 44:3-21.   |                |
|                                 |                       | ALLAKHVERDI <i>et al.</i> , "Inhibition of Antigen-induced Eosinophilia and Airway Hyperresponsiveness by Antisense Oligonucleotides Directed against the Common $\beta$ Chain of IL-3, IL-5, GM-CSF Receptors in a Rat Model of Allergic Asthma", 2002, <i>Am. J. Respir. Crit. Care Med.</i> 165:1015-1021.                     |                |
|                                 |                       | ANDREOLA <i>et al.</i> , "DNA aptamers selected against the HIV-1 RNase H display in vitro antiviral activity", 2001, <i>Biochemistry</i> , 40:10087-10094.   |                |
|                                 |                       | BAKER <i>et al.</i> , "2-O-(2-Methoxy)ethyl-modified Anti-intercellular Adhesion Molecule 1 (ICAM-1) Oligonucleotides Selectively Increase the ICAM-1 mRNA Level and Inhibit Formation of the ICAM-1 Translation Initiation Complex in Human Umbilical Vein Endothelial Cells", 1997, <i>J. Biol. Chem.</i> 272 (18):11994-12000. |                |
|                                 |                       | BALL <i>et al.</i> , "Clinical Potential of Respirable Antisense Oligonucleotides (RASONS) in Asthma", 2003, <i>Am. J. Pharmacogenomics</i> 3 (2):97-106.   |                |
|                                 |                       | BANKS <i>et al.</i> , "Delivery across the Blood-Brain Barrier of Antisense Directed against Amyloid $\beta$ : Reversal of Learning and Memory Deficits in Mice Overexpressing Amyloid Precursor Protein", 2001, <i>J. Pharmacol. Exp. Ther.</i> 297 (3):1113-1121.   |                |
|                                 |                       | BARDOS <i>et al.</i> , "Structure-Activity Relationships and Mode of Action of 5-Mercapto-Substituted Oligo- and Polynucleotides as Antitemplates Inhibiting Replication of Human Immunodeficiency Virus Type 1", 1992, <i>Antimicrob. Agents and Chemother.</i> 36 (1):108-114.  |                |

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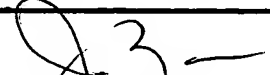
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|   |   |    |    | Filing Date              | September 12, 2003     |
|   |   |    |    | First Named Inventor     | Andrew Vaillant et al. |
|   |   |    |    | Art Unit                 | 1635                   |
|   |   |    |    | Examiner Name            | Jane J. ZARA           |
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| J3                              |                       | BARRET <i>et al.</i> , "Evaluation of Quinacrine Treatment for Prion Diseases", 2003, <i>J. of Virol.</i> 77 (15):8462-8469.   |                |
|                                 |                       | BATE <i>et al.</i> , "Squalestatin Cures Prion-infected Neurons and Protects Against Prion Neurotoxicity", 2004, <i>J. of Biol. Chem.</i> 279 (15):14983-14990.  |                |
|                                 |                       | BOUSSIF <i>et al.</i> , "A versatile Vector for Gene and Oligonucleotide Transfer into Cells in Culture and in vivo: Polyethylenimine", 1995, <i>Proc. Natl. Acad. Sci. USA.</i> 92 (16):7297-7301.  |                |
|                                 |                       | BRIGGER <i>et al.</i> , "Poly(ethylene glycol)-Coated Hexadecylcyanoacrylate Nanospheres Display a Combined Effect for Brain Tumor Targeting", 2002, <i>J. Pharmacol. Exp. Ther.</i> 303 (3):928-936.  |                |
|                                 |                       | CASPER, "Discovery of a Novel Target for Potential Cancer Therapy", Joint Bayer Science Forum – ACS November 24 <sup>th</sup> Dinner Meeting, 2003, The FILTERPAPER, Andy Edelbrock Bayer Corporation, page 3 (abstract).                                      |                |
|                                 |                       | CAUGHEY <i>et al.</i> , "Sulfated Polyanion Inhibition of Scrapie-Associated PrP Accumulation in Cultured Cells", 1993, <i>J. Virol.</i> 67 (2):643-650.   |                |
|                                 |                       | CHEN <i>et al.</i> , "Antisense Oligonucleotides Demonstrate a Dominant Role of c-Ki-RAS Proteins in Regulating the Proliferation of Diploid Human Fibroblasts", 1996, <i>J. Biol. Chem.</i> 271 (45):28259-28265.   |                |
|                                 |                       | CHEONG <i>et al.</i> , "Structure of influenza virus panhandle RNA studied by NMR spectroscopy and molecular modeling", 1999, <i>Nuc. Acids. Res.</i> 27 (5): 1392-1397.   |                |
|                                 |                       | CHIANG <i>et al.</i> , "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms", 1991, <i>J. Biol. Chem.</i> 266 (27):18162-18171.   |                |
|                                 |                       | CIOFFI <i>et al.</i> , "Selective Inhibition of A-Raf and C-Raf mRNA Expression by Antisense Oligodeoxynucleotides in Rat Vascular Smooth Muscle Cells: Role of A-Raf and C-Raf in Serum-Induced Proliferation", 1997, <i>Mol. Pharmacol.</i> 51:383-389.      |                |

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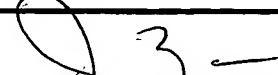
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| g z                             |                       | CROOKE et al., "In Vitro Toxicological Evaluation of ISIS 1082, a Phosphorothioate Oligonucleotide Inhibitor of Herpes Simplex Virus", 1992, <i>Antimicrob. Agents Chemother.</i> 36 (3):527-532.  |                |
|                                 |                       | DASS, "Vehicles for oligonucleotide delivery to tumours", 2002, <i>Journal of Pharmacy and Pharmacology</i> 54:3-27.   |                |
|                                 |                       | DASS, "Liposome-Mediated Delivery of Oligodeoxynucleotides In Vivo", 2002, <i>Drug Delivery</i> , 9:169-180.   |                |
|                                 |                       | DHEUR et al., "Polyethylenimine but Not Cationic Lipid Improves Antisense Activity of 3'-Capped Phosphodiester Oligonucleotides", 1999, <i>Antisense &amp; Nucleic Acid Drug Development</i> , 9:515-525.  |                |
|                                 |                       | DOH-URA et al., "Treatment of Transmissible Spongiform Encephalopathy by Intraventricular Drug Infusion in Animal Models", 2004, <i>J. Virol.</i> 78 (10):4999-5006.   |                |
|                                 |                       | ELBASHIR et al., "RNA interference is mediated by 21- and 22-nucleotide RNAs", 2001, <i>Genes &amp; Development</i> 15:188-200.  |                |
|                                 |                       | ELBASHIR et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells", 2001, <i>Nature</i> 411:494-498.   |                |
|                                 |                       | FINOTTO et al., "Local administration of antisense phosphorothioate oligonucleotides to the c-kit ligand, stem cell factor, suppresses airway inflammation and IL-4 production in a murine model of asthma", 2001, <i>J. Allergy Clin. Immunol.</i> 107 (2):279-286. |                |
|                                 |                       | FISET et al., "Modulation of allergic response in nasal mucosa by antisense oligodeoxynucleotides for IL-4", 2003, <i>J. Allergy Clin. Immunol.</i> 111 (3):580-586.   |                |
|                                 |                       | GARRETT et al., "In vivo use of oligonucleotides to inhibit choroidal neovascularisation in the eye", 2001, <i>J. Gene Med.</i> 3:373-383.   |                |

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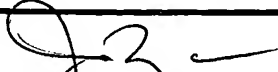
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| JZ                              |                       | GORLACH <i>et al.</i> , "Antisense repression in <i>Cryptococcus neoformans</i> as a laboratory tool and potential antifungal strategy", 2002, <i>Microbiology</i> 148:213-219.   |                |
|                                 |                       | GRIGORIEV <i>et al.</i> , "Effects of the polyene antibiotic derivative MS-8209 on the astrocyte lysosomal system of scrapie-infected hamsters", 2002, <i>J. Mol. Neurosci.</i> 18:271-281.   |                |
|                                 |                       | HARBOTH <i>et al.</i> , "Identification of essential genes in cultured mammalian cells using small interfering RNAs", 2001, <i>Journal of Cell Science</i> 114 (24) 4557-4565.  |                |
|                                 |                       | HORVATH <i>et al.</i> , "Potent inhibition of HIV-1 entry by (s <sup>4</sup> dU) <sub>35</sub> ", 2005, <i>Virology</i> 334:214-223.  |                |
|                                 |                       | HUGHES <i>et al.</i> , "The cellular delivery of antisense oligonucleotides and ribozymes", 2001, <i>Drug Discovery Today</i> . 6 (6) :303-315.   |                |
|                                 |                       | HUWYLER <i>et al.</i> , "Brain drug delivery of small molecules using immunoliposomes", 1996, <i>Proc. Natl. Acad. Sci. USA</i> 93:14164-14169.   |                |
|                                 |                       | INOUE <i>et al.</i> , "Synthesis and properties of novel nucleic acid probes", 1985, <i>Symposium Series - Nucleic Acids Research</i> No. 16:165-168.   |                |
|                                 |                       | INOUE <i>et al.</i> , "Sequence-dependent hydrolysis of RNA using modified oligonucleotide splints and RNase H", 1987, <i>FEBS Letters</i> 215 (2) :327-330.  |                |
|                                 |                       | JAASKELAINEN <i>et al.</i> , "A lipid carrier with a membrane active component and a small complex size are required for efficient cellular delivery of anti-sense phosphorothioate oligonucleotides", 2000, <i>European Journal of Pharmaceutical Sciences</i> 10:187-193. |                |
|                                 |                       | KANAGARATNAM <i>et al.</i> , "Malaria merozoite surface protein antisense oligodeoxynucleotides lack antisense activity but function as polyanions to inhibit red cell invasion", 1998, <i>Int. J. Biochem. Cell Biol.</i> 30:979-985.                                      |                |
|                                 |                       | KOCISKO <i>et al.</i> , "New Inhibitors of Scrapie-Associated Prion Protein Formation in a Library of 2,000 Drugs and Natural Products", 2003, <i>J. Virol.</i> 77 (19) :10288-10294.   |                |

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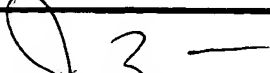
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|                                 |  | KURRECK, "Antisense technologies. Improvement through novel chemical modifications", 2003, <i>Eur. J. Biochem.</i> 270:1628-1644.  |                |
|                                 |  | KUWASAKI <i>et al.</i> , "Inhibition of human immunodeficiency virus 1 replication <i>in vitro</i> by a self-stabilized oligonucleotide with 2'-O-methyl-guanosine-uridine quadruplex motifs", 2003, <i>J. Antimicrob. Chemother.</i> 51:813-819.              |                |
|                                 |  | LAU <i>et al.</i> , "Abrogation of c-Raf expression induces apoptosis in tumor cells", 1998, <i>Oncogene</i> 16:1899-1902.   |                |
|                                 |  | LEUNG and SHAH, in: <i>Controlled Release of drugs: Polymers and aggregate systems</i> , Rosoff, M., Ed., 1989, VCH Publishers, New York, pages 185-215.   |                |
|                                 |  | LUO <i>et al.</i> , "Inhibition of influenza viral polymerases by minimal viral RNA decoys", 1997, <i>J. Gen. Virol.</i> 78: 2329-2333.  |                |
|                                 |  | de MERGNY <i>et al.</i> , "Kinetics and thermodynamics of i-DNA formation: phosphodiester versus modified oligodeoxynucleotides", 1998, <i>Nucleic Acids Res.</i> 26 (21): 4797-4803.  |                |
|                                 |  | de MONBRISON <i>et al.</i> , "Introducing antisense oligonucleotides into <i>Pneumocystis carinii</i> ", 2002, <i>J. Microbiol. Methods</i> 50:211-213.  |                |
|                                 |  | MONIA <i>et al.</i> , "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression", 1993, <i>J. Biol. Chem.</i> 268 (19):14514-14522.  |                |
|                                 | MORASSUTTI <i>et al.</i> , "Effect of phosphorothioate modifications on the ability of GTn oligodeoxynucleotides to specifically recognize single-stranded DNA-binding proteins and to affect human cancer cellular growth" 1999, <i>Biochimie</i> 81:1115-1122. |  |                |

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| 83                              |                       | MOU and GRAY, "The high binding affinity of phosphorothioate-modified oligomers for Ff gene 5 protein is moderated by the addition of C-5 propyne or 2'-O-methyl modifications", 2002, <i>Nucleic Acids Res.</i> 30 (3):749-758.                               |                |
|                                 |                       | NAKAJIMA et al., "Results of Quinacrine Administration to Patients with Creutzfeldt-Jakob Disease", 2004, <i>Dement. Geriatr. Cogn. Disord.</i> 17:158-163.  |                |
|                                 |                       | NOGUCHI et al., "Remarkable induction of apoptosis in cancer cells by a novel cationic liposome complexed with a bcl-2 antisense oligonucleotide", 2003, <i>Journal of Controlled Release</i> 88:313-320.  |                |
|                                 |                       | NOONPAKDEE et al., "Inhibition of <i>Plasmodium falciparum</i> proliferation in vitro by antisense oligodeoxynucleotides against malarial topoisomerase II", 2003, <i>Biochem. and Biophys. Res. Commun.</i> 302:659-664.                                      |                |
|                                 |                       | O'BRIEN et al., "Antisense BCR-ABL Oligomers Cause Non-Specific Inhibition of Chronic Myeloid Leukemia Cell Lines", 1994, <i>Leukemia</i> 8 (12):2156-2162.  |                |
|                                 |                       | OMORI et al., "Targeting of post-ischemic cerebral endothelium in rat by liposomes bearing polyethylene glycol-coupled transferrin", 2003, <i>Neurol. Res.</i> 25:275-279.   |                |
|                                 |                       | Orum et al., "Locked nucleic acids: A promising molecular family for gene-function analysis and antisense drug development", 2001, <i>Current Opinion in Molecular Therapeutics</i> 3 (3):239-243.   |                |
|                                 |                       | PAN et al., "Isolation of virus-neutralizing RNAs from a large pool of random sequences", 1995, <i>Proc. Natl. Acad. Sci. USA</i> 92:11509-11513.  |                |
|                                 |                       | PAPUCCI et al., "Phosphodiester Oligonucleotides Inhibit Mitosis and Trigger Apoptosis by a Non-Antisense, p53-Mediated Mechanism", 2002, <i>Antisense &amp; Nucleic Acid Drug Development</i> 12:21-31.   |                |
|                                 |                       | PEREZ et al., "Sequence-independent induction of Sp1 transcription factor activity by phosphorothioate oligodeoxynucleotides", 1994, <i>Proc. Natl. Acad. Sci. USA</i> 91:5957-5961.   |                |
|                                 |                       | POLI et al., "In vitro Evaluation of the Anti-prionic Activity of Newly Synthesized Congo Red Derivatives", 2003, <i>Arzneim.-Forsch./Drug Res.</i> 53 (12):875-888.   |                |

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|   |    |    | Filing Date              | September 12, 2003     |              |
|   |    |    | First Named Inventor     | Andrew Vaillant et al. |              |
|   |    |    | Art Unit                 | 1635                   |              |
|   |    |    | Examiner Name            | Jane J. ZARA           |              |
| Sheet   | 11 | of | 13                       | Attorney Docket Number | 16051-6US CC |

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| JZ                              |  | PRIOLA <i>et al.</i> , "Porphyrin and Phthalocyanine Antiscruple Compounds", 2000, <i>Science</i> 287: 1503-1506.  |                |
|                                 |  | PROSKE <i>et al.</i> , "Prion-Protein-Specific Aptamer Reduces PrP <sup>Sc</sup> Formation", 2002, <i>Chemic. Biol.Chem.</i> 3:717-725.  |                |
|                                 |  | RAMAZEILLES <i>et al.</i> , "Antisense phosphorothioate oligonucleotides: Selective killing of the intracellular parasite <i>Leishmania amazonensis</i> ", 1994, <i>Proc. Natl. Acad. Sci. USA</i> 91:7859-7863.   |                |
|                                 |  | RHIE <i>et al.</i> , "Characterization of 2'-fluoro-RNA aptamers that bind preferentially to disease-associated conformations of prion protein and inhibit conversion", 2003, <i>J. Biol. Chem.</i> , 278 (41):39697-39705.                                    |                |
|                                 |  | Rieger, in: <i>Pharmaceutical Dosage Forms</i> , Lieberman, Rieger and Banker (Eds), 1988, Marcel Dekker, INC., New York, NY, Vol. 1, pp. 285-366  |                |
|                                 |  | ROH <i>et al.</i> , "Down-Regulation of HER2/ <i>neu</i> Expression Induces Apoptosis in Human Cancer Cells That Overexpress HER2/ <i>neu</i> ", 2000, <i>Cancer Research</i> 60:560-565.  |                |
|                                 |  | ROSOFF, in: <i>Pharmaceutical Dosage Forms</i> , Lieberman, Rieger and Banker (Eds), 1988, Marcel Dekker, INC., New York, NY, Vol. 1, pp.245-282.  |                |
|                                 |  | SCHMIDT <i>et al.</i> , "Drug targeting by long-circulating liposomal glucocorticosteroids increases therapeutic efficacy in a model of multiple sclerosis", 2003, <i>Brain</i> 126 :1895-1904.  |                |
|                                 |  | SHYNG <i>et al.</i> , "Sulfated Glycans Stimulate Endocytosis of the Cellular Isoform of the Prion Protein, PrP <sup>C</sup> , in Cultured Cells", 1995, <i>J. Biol. Chem.</i> 270 (50) :30221-30229.  |                |
|                                 | SIERAKOWSKA <i>et al.</i> , "Repair of thalassemic human $\beta$ -globin mRNA in mammalian cells by antisense oligonucleotides", 1996, <i>Proc. Natl. Acad. Sci. USA</i> 93:12840-12844. |  |                |

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|   |    |    |    | First Named Inventor     | Andrew Vaillant et al. |
|   |    |    |    | Art Unit                 | 1635                   |
|   |    |    |    | Examiner Name            | Jane J. ZARA           |
| Sheet   | 12 | of | 13 | Attorney Docket Number   | 16051-6US CC           |

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| J3                              |                       | SMETSERS et al., "An antisense Bcr-Abl phosphodiester-tailed methylphosphonate oligonucleotide reduces the growth of chronic myeloid leukaemia patient cells by a non-antisense mechanism", 1997, <i>British Journal of Haematology</i> 96:377-381.            |                |
|                                 |                       | SUPATTAPONE et al., "Branched Polyamines Cure Prion-Infected Neuroblastoma Cells", 2001, <i>J. Virol.</i> 75 (7):3453-3461.  |                |
|                                 |                       | TCHATALBACHEV et al., "The packaging signal of influenza viral RNA molecules", 2001, <i>RNA</i> 7: 979-989.  |                |
|                                 |                       | UHLMANN and PEYMAN, "Antisense Oligonucleotides: A New Therapeutic Principle", 1990, <i>Chemical Reviews</i> 90 (4):544-584.   |                |
|                                 |                       | VAN DEVENTER et al., "A randomised, controlled, double blind, escalating dose study of alicaforsen enema in active ulcerative colitis", 2004, <i>Gut</i> . 53:1646-1651.   |                |
|                                 |                       | VINOGRADOV et al., "Nanogels for Oligonucleotide Delivery to the Brain", 2004, <i>Bioconjug. Chem.</i> 15:50-60.   |                |
|                                 |                       | WANG et al., "Sequence-Independent Inhibition of In Vitro Vascular Smooth Muscle Cell Proliferation, Migration, and In Vivo Neointimal Formation by Phosphorothioate Oligodeoxynucleotides", 1996, <i>J. Clin. Invest.</i> 98 (2):443-450.                     |                |
|                                 |                       | WHITE et al., "Inhibition of the Multiple Antibiotic Resistance ( <i>mar</i> ) Operon in <i>Escherichia coli</i> by Antisense DNA Analogs", 1997, <i>Antimicrobial Agents and Chemotherapy</i> 41 (12):2699-2704.  |                |
|                                 |                       | WHITE et al., "Development of novel methods for delivering therapeutic oligonucleotides to the central nervous system", 2003, <i>Society for Neuroscience</i> , Program #325.5, Abstract.  |                |
| ✓                               |                       | WHITE et al., "Antisense oligonucleotide treatments for psoriasis", 2004, <i>Expert. Opin. Biol. Ther.</i> 4(1):75-81.   |                |

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| JZ                              |                          | XU et al., "Inhibition of DNA Replication and Induction of S Phase Cell Cycle Arrest by G-rich Oligonucleotides", 2001, <i>The Journal of Biological Chemistry</i> 276 (46):43221-43230.  |                |
|                                 |                          | YANG et al., "Construction and selection of bead-bound combinatorial oligonucleoside phosphorothioate and phosphorodithioate aptamer libraries designed for rapid PCR-based sequencing", 2002, <i>Nucl. Acids Res.</i> 30 (23):1-8.                                     |                |
|                                 |                          | YU et al., "Hybrid Oligonucleotides: Synthesis, Biophysical Properties, Stability Studies, and Biological Activity", 1996, <i>Bioorganic. Med. Chem.</i> 4 (10):1685-1692.  |                |
|                                 |                          | YU et al., "Prediction of Clinical Responses in a Simulated Phase III Trial of Crohn's Patients Administered the Antisense Phosphorothioate Oligonucleotide ISIS 2302: Comparison of Proposed Dosing Regimens", 2003, <i>Antisense Nucleic Acid Drug Dev.</i> 13:57-66. |                |
|                                 |                          | ZELLWEGER et al., "Antitumor Activity of Antisense Clusterin Oligonucleotides Is Improved in Vitro and in Vivo by Incorporation of 2'-O-(2-Methoxy)Ethyl Chemistry", 2001, <i>J. Pharmacol. and Experimental Therapeutics</i> 298 (3):934-940.                          |                |
|                                 |                          | ZHANG et al., "A Simple Glycol Nucleic Acid", 2005, <i>J. Am. Chem. Soc.</i> 127:4174-4175.   |                |
|                                 |                          | ZHANG et al., "The Study on Brain Targeting of the Amphotericin B Liposomes", 2003, <i>J. Drug. Target.</i> 11 (2):117-122.   |                |
|                                 |                          | ZHANG et al., "Global Non-Viral Gene Transfer to the Primate Brain Following Intravenous Administration", 2003, <i>Mol. Ther.</i> 7 (1):11-18.  |                |
|                                 |                          | <i>The Concise Encyclopedia of Polymer Science and Engineering</i> , Jacqueline I. Kroschwitz, 1998, ISBN: 0-471-31856-6, 1341 pages, pp.858-859.   |                |
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